UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/759,207 | 01/16/01 | PECKER I | 00/21505 |

HM12/0925

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| EXAMINER | |
|---|---|
| DECLOUX, A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

**DATE MAILED:** 09/25/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/759,207 | Pecker et al. |
| **Examiner** | **Art Unit** |
| DeCloux, Amy | 1644 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 1-10 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-10 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

## DETAILED ACTION

1. Formal drawings and/or photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the attached PTO-948 form.

2. Applicant should amend the first line of the specification to update the status of the priority documents.

3. *35 U.S.C. § 101* reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

4. Claims 1-10 are rejected under 35 U.S.C. 101 because, the claimed invention is directed to non-statutory subject matter. "An antibody", as recited in claims 1-10 would read on antibodies in human patients which is a naturally-occurring product of nature and thus constitutes non-statutory subject matter. Inserting "isolated" before "antibody" would overcome this rejection.

5. Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well established utility.

The heparanase binding antibody recited in the instant claims has the specific, substantial and well established asserted utility of identifying heparanase in a tumor as disclosed on page 34 of the instant specification because tumor cells have a higher level of heparanase as disclosed in the instant specification. However said utility is applicable only if the antibody is directed against human heparanase and not bacterial heparanase. There is no asserted utility for an antibody which binds a bacterial heparanase. Thus the Applicants have failed to assert and provide a specific utility for the claimed invention, embodied as an antibody to bacterial heparanase.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and

process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Applicant is advised that should claim 3 be found allowable, claim 8 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Specifically, the claims encompass the same antibody since they are drawn to an antibody obtained by the same process.

9. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-10 are drawn to an antibody specifically binding at least one epitope of a heparanase protein and an antibody elicited by at least one epitope of a heparanase protein. The instant specification discloses on page 32 that heparanase has endoglycosidase hydrolyzing activity which is specific for heparin or heparin sulfate proteoglycan substrates, as opposed to bacterial enzymes which degrade heparin or heparin sulfate by means of beta elimination. However, the instant claims recite an antibody specifically binding "a heparanase protein" , and does not distinguish between different subsets (ie bacterial or eucaryotic) of heparanase proteins. Further the instant specification discloses no description of the required structural features that would be critical for said functional features of said polypeptides, or of the conserved regions that would be critical for these features. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polypeptides encompassed. Since the applicants have not disclosed a heparanase other than the human heparanase of SEQ ID NO:1 and mouse heparanase, the invention encompassing an antibody directed to heparanase (other than

SEQ ID NO:1 and mouse heparanase), is not adequately described.

It is noted that a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

10. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibody specifically binding at least one epitope of a heparanase protein and an isolated antibody elicited by at least one epitope of a heparanase protein, does not reasonably provide enablement for the broader recitation of an isolated antibody specifically binding at least one epitope of any heparanase protein and an isolated antibody elicited by at least one epitope of a any heparanase protein (other than SEQ ID NO:1 and a mouse heparanase). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in the instant claims without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims.

The instant specification provides enablement only for an isolated antibody specifically binding at least one epitope of a heparanase protein and an isolated antibody elicited by at least one epitope of a heparanase protein, wherein said heparanase protein is that encoded by SEQ ID NO:1 and one found in mouse. The instant specification provides insufficient guidance for an isolated antibody specifically binding at least one epitope of a heparanase protein or an isolated antibody elicited by at least one epitope of a heparanase protein, wherein said heparanase is any other heparanase other than that encoded by SEQ ID NO:1 and one found in mouse. The applicants have failed to describe any other heparanase in the instant specification. However even if one argues that another heparanase protein, known or unknown, would have a similar amino acid structure as that encoded by SEQ ID NO:1 and one found in mouse, there is insufficient guidance and direction in the instant specification that said antibody would bind since Abaza et al (J.

Of Protein Chemistry, 11(5):433-444, 1992) show that even a single amino acid difference in an antigen may effect antibody binding by teaching that an amino acid substitution of myoglobin outside the epitope recognized by a monoclonal antibody causes the myoglobin to be unreactive with said antibody, (see entire article, especially the Abstract). Therefore predicting which heparanase molecules other than that encoded by SEQ ID NO:1 and one found in mouse, will be capable of interacting with the instantly recited antibody would require undue experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

11. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-2, 4-7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by WO9119197.

The '197 patent teaches an antibody to human and mouse heparanase (see entire patent, including the Abstract). Said antibody includes polyclonal antibody as taught in claim 3 of '197, and said antibody reacts with native heparanase as taught and illustrated by Figure 7 of '197 that shows the binding of said antibody against native heparanase in tumor cells. Although '197 does not specifically teach an antibody to recombinant heparanase protein, it is noted that said antibody would be the same regardless if it were elicited or made by immunization with a recombinant or nonrecombinant heparanase protein. It is noted that the method of making a product is not given patentable weight in a product claim. Therefore, the reference teachings anticipate the claimed invention.

13. The following is a quotation of *35 U.S.C. § 103* which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under *subsection (f) or (g)* of *section 102* of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 3 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO9119197 in view of Edwards (Biochem. J. (1981) 200:1-10).

WO9119197 teaches as above. '197 further teaches that antibodies against heparanase can be used to detect heparin sulfate endoglycosidase in tumor cells and the amounts of heparanase antigens may be used to design appropriate therapeutic courses (see entire article, especially the Abstract). However, '197 does not teach a monoclonal antibody against heparanase.

Edwards teaches a way to construct hybridomas that make an antibody to an antigen of choice encompassing exposing cells capable of producing antibodies to heparanase, fusing said antibody producing cells to myeloma cells generating hybridomas that secrete antibodies, and screening said antibodies to find one that specifically binds the antigen of choice (see entire article, especially page 1 and column 1 of page 2). Edwards also teaches that monoclonal antibodies have advantages over polyclonal antibodies, including the advantages of reproducibility of the epitope

recognition and binding affinity to a given epitope by an individual monoclonal antibody, (see entire article, especially Table 2)

Therefore it would have been obvious to one of ordinary skill in the art who wanted to use an antibody to heparanase as part of a treatment method in cancer patients, to have made a monoclonal antibody against heparanse, because '197 teaches a polyclonal antibodies against heparanase may be used to design appropriate therapeutic courses in cancer patients, and because Edwards teaches the advantages of monoclonal antibodies as compared to polyclonal antibodies in terms of the monoclonal antibody's reproducibility of the epitope recognition and binding affinity to a given epitope, and this reproducibility would be advantageous in terms of providing reproducible detection methods and for determining therapeutic treatments.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D.
Patent Examiner,
September 24, 2001

David A Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
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